DEPARTMENT OF HEALTH AND HUMAN SERVICES

Agency for Healthcare Research and Quality

Supplemental Evidence and Data Request on Radiation Therapy for Bone Metastases

AGENCY: Agency for Healthcare Research and Quality (AHRQ), HHS.

ACTION: Request for Supplemental Evidence and Data Submissions.

SUMMARY: The Agency for Healthcare Research and Quality (AHRQ) is seeking scientific information submissions from the public. Scientific information is being solicited to inform our review on *Radiation Therapy for Bone Metastases,* which is currently being conducted by the AHRQ's Evidence-based Practice Centers (EPC) Program. Access to published and unpublished pertinent scientific information will improve the quality of this review.

DATES: *Submission Deadline* on or before [INSERT DATE 30 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER].

ADDRESSES:

E-mail submissions: epc@ahrq.hhs.gov

Print submissions:

Mailing Address:

Center for Evidence and Practice Improvement

Agency for Healthcare Research and Quality

ATTN: EPC SEADs Coordinator

5600 Fishers Lane

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Rockville, MD 20857

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FOR FURTHER INFORMATION CONTACT:

Jenae Benns, Telephone: 301-427-1496 or Email: epc@ahrq.hhs.gov.

SUPPLEMENTARY INFORMATION: The Agency for Healthcare Research and Quality has commissioned the Evidence-based Practice Center (EPC) Program to complete a review of the evidence for *Radiation Therapy for Bone Metastases.* AHRQ is conducting this systematic review pursuant to Section 902 of the Public Health Service Act, 42 U.S.C. 299a.

The EPC Program is dedicated to identifying as many studies as possible that are relevant to the questions for each of its reviews. In order to do so, we are supplementing the usual manual and electronic database searches of the literature by requesting information from the public (e.g., details of studies conducted). We are looking for studies that report on Radiation Therapy for Bone Metastases*,* including those that describe adverse events. The entire research protocol is available online at:

https://effectivehealthcare.ahrq.gov/products/radiation-therapy-bone-metastases/protocol

This is to notify the public that the EPC Program would find the following information on Radiation Therapy for Bone Metastases helpful:

- A list of completed studies that your organization has sponsored for this indication. In the list, please *indicate whether results are available on ClinicalTrials.gov along with the ClinicalTrials.gov trial number*.
    - *For completed studies that do not have results on ClinicalTrials.gov*, a summary, including the following elements: study number, study period, design, methodology, indication and diagnosis, proper use instructions, inclusion and exclusion criteria, primary and secondary outcomes, baseline characteristics, number of patients screened /eligible /enrolled /lost to follow-up /withdrawn /analyzed, effectiveness/efficacy, and safety results.
- *A list of ongoing studies that your organization has sponsored for this indication*. In the list, please provide the ClinicalTrials.gov trial number or, if the trial is not registered, the protocol for the study including a study number, the study period, design, methodology, indication and diagnosis, proper use instructions, inclusion and exclusion criteria, and primary and secondary outcomes.
- Description of whether the above studies constitute *ALL Phase II and above clinical trials* sponsored by your organization for this indication and an index outlining the relevant information in each submitted file.

Your contribution is very beneficial to the Program. Materials submitted must be publicly available or able to be made public. Materials that are considered confidential; marketing materials; study types not included in the review; or information on

indications not included in the review cannot be used by the EPC Program. This is a voluntary request for information, and all costs for complying with this request must be borne by the submitter.

The draft of this review will be posted on AHRQ's EPC Program website and available for public comment for a period of 4 weeks. If you would like to be notified when the draft is posted, please sign up for the e-mail list at: https://www.effectivehealthcare.ahrq.gov/email-updates.

The systematic review will answer the following questions. This information is provided as background. AHRQ is not requesting that the public provide answers to these questions.

Key Questions (KQ)

KQ 1: What is the effectiveness and what are the harms of external beam radiation therapy (EBRT) in the palliative treatment of bone metastases in symptomatic adults when combined with additional therapies (e.g., surgery, radionuclide therapy, bisphosphonate therapy, ablation kyphoplasty/vertebroplasty) compared with EBRT alone?

KQ 2: For symptomatic adults with bone metastases who will receive initial radiation for palliation, what is the comparative effectiveness and what are the comparative harms of dose-fractionation schemes and techniques for delivery (e.g., three-dimensional conformal radiation therapy, stereotactic body radiation)?

KQ 3: For symptomatic adults with bone metastases who will receive re-irradiation for palliation, what is the comparative effectiveness and what are the comparative harms of dose-fractionation schemes and techniques for delivery (e.g., three-dimensional conformal radiation therapy, stereotactic body radiation)?

Contextual Questions (CQ):

CQ 1: What are common barriers and facilitators to implementing guidance in radiation oncology, specifically related to palliative radiation for metastatic bone disease (MBD)?

CQ 2: What strategies could be used to promote the use and implementation of guidance in radiation oncology, specifically related to palliative radiation for MBD?

CQ 3: In symptomatic patients considered for palliative radiation therapy for MBD, to what extent does patient financial distress/hardship differ between EBRT dose/fraction schemes or technique?

PICOTS (Populations, Interventions, Comparators, Outcomes, Timing, and Setting)

	Inclusion	**Exclusion**
Population	**KQ 1:** Symptomatic adults with cancer that has metastasized to the bone. **KQ 2:** Symptomatic adults with bone metastases who will receive initial palliative radiation **KQ 3:** Symptomatic adults with bone metastases who will receive re-radiation for palliation **For all KQ:** Consider patient and clinical characteristics (e.g., age, sex, social determinants of health, primary tumor histology, site of metastases)	• Patients <18 years old • Asymptomatic patients • Patients with primary bone tumors
Interventions	**KQ 1:** External beam radiation therapy for the palliative management of bone metastasis *with co-interventions*, additional therapies (e.g., .,	**KQ 1, 2, 3:** Proton beam therapy

	surgery, radionuclide therapy, bisphosphonate therapy, ablation, kyphoplasty/vertebroplasty) **KQ 2 and KQ 3:** Comparisons of dose-fractionation schemes for EBRT, comparisons of EBRT techniques (e.g., conventional RT vs. SBRT, SBRT vs. IMRT)	**KQ1:** Brachytherapy
Comparators	**KQ 1:** No cointervention (i.e., EBRT alone) **KQ 2 and KQ 3:** Comparisons of dose-fractionation schemes, comparisons of EBRT modalities/techniques	
Outcomes	**Effectiveness:** Primary outcomes • Pain (level and duration) • Skeletal function • Relief of spinal cord compression • Quality of life Additional (secondary) outcomes • Local recurrence • Fracture prevention • Overall survival • Need for re-radiation • Use of pain medication, need for other interventions for pain relief **Harms and adverse events** Harms (e.g., rate of radiation/treatment toxicity, radiation-induced fracture rates, reduced mobility, reduced independence), adverse events (pain flare, radiation recall, fatigue, skin changes, etc.)	• Non-validated measurement instruments for clinician or patient rated outcomes (e.g., pain, function, HRQOL)
Timing	Any (timing may depend on treatments provided and outcomes assessed)	None
Setting	Any	None
Study design and publication dates	**All KQ:** Focus will be on the best evidence available that permits direct comparisons to answer key questions RCTs will be initially sought; in the absence of RCTs, prospective comparative studies that control for confounding will be considered; if no comparative prospective studies are available, retrospective comparative studies that control for confounding will be considered. In the absence of comparative studies, single arm (e.g., case series, pre-post studies) may be considered	**GENERAL** • Dosimetry modeling studies • Non-human studies • NRSI for effectiveness if RCTs are available • Studies with <10 patients per arm • Single arm studies (unless no comparative studies); if used, exclude studies of <10 patients • Case reports

	For evaluation of harms, comparative cohort and case-control studies will be included; we will focus on studies specifically designed to evaluate harms. Studies of at least 10 patients per treatment arm	**Publication dates**: Prior to 1985 **Publication types:** Conference abstracts or proceedings, editorials, letters, white papers, citations that have not been peer-reviewed, single site reports of multi-site studies

EBRT = external beam radiation therapy; HRQOL = health-related quality of life; IMRT = intensity modulated radiation therapy; KQ = key question; NRSI = nonrandomized studies of intervention; RCT = randomized controlled trial; RT = radiation therapy; SBRT = stereotactic radiation therapy.

Dated: July 6, 2022.

Mamatha Pancholi,

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Chief Data Officer.

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